Reply to Office action of July 31, 2007

## Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

## Listing of Claims:

Claim 1 (Original): A multiparameter method of screening for the diagnosis, the prevention or the treatment of atherosclerosis-related coronary heart disease (CHD) or stroke comprising;

defining the disease as atherosclerosis-related CHD or stroke;

defining the normal as free from said disease;

defining the following parameters as

atherosclerotic parameters consisting of c =

the Low-density lipoprotein (LDL) concentration

parameter in mg/dL or c = the C-reactive

protein (CRP) concentration parameter in mg/L,

p = the blood systolic pressure parameter in

mmHg or p = the blood diastolic pressure

parameter in mmHg, f = the heart rate parameter

in s<sup>-1</sup>, a = the radius parameter along arterial

radius in cm, T = the temperature parameter of

Reply to Office action of July 31, 2007

blood plasma in °C,  $\alpha$  = the angle parameter between gravity and the mean velocity of blood fluid in arterial vessels in degree and z = the axial position parameter of diffusion flux along the inner wall in the axial direction of arterial vessels in cm, called the diffusion length;

an individual having the measured values of said atherosclerotic parameters of the following expressions:

$$J = Ac^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} \left( \frac{g\cos\alpha + fu}{z} \right)^{\frac{2}{9}}$$
 (1.1)

or

$$J = Bc^{\frac{11}{9}} p^{\frac{1}{3}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}}$$
 (1.2)

and

$$J = E c^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}} (\cos \alpha)^{\frac{2}{9}}$$
 (1.3)

wherein J = the mass transfer flux in 10<sup>-5</sup> g/(cm<sup>2</sup>s), A, B and E = the constants of conversion factors, v = the eddy velocity of blood fluid in arterial vessels in cm/s, u = the mean velocity of the blood fluid in cm/s, D = the diffusion coefficient in cm<sup>2</sup>/s, and g = the gravitational acceleration in cm/s<sup>2</sup>;

the individual having the normal values of said

Reply to Office action of July 31, 2007

atherosclerotic parameters;

- determining the disease risks yielded by the differences between said measured values and said normal values of said atherosclerotic parameters;
- adding all said disease risks together yields a total risk of said disease;
- determining a disease risk level containing said total risk of said disease;
- selecting an atherosclerotic risk factor related to an atherosclerotic parameter that is the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease;
- selecting a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease;
  - selecting a greater concentration level between the LDL level in serum and the CRP level in

Reply to Office action of July 31, 2007

blood plasma so as to result in said greater level as a secondary therapy target of said disease;

determining a relative ratio between currently said total risk and previously said total risk so as to yield said relative ratio as a therapeutic efficacy of said disease;

repeating above-mentioned said methods until said disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke; and

above-mentioned said methods are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods and to output a result of said methods to a display or a memory or another computer on a network, or to a user.

Claim 2 (currently amended): A method as in claim 1, wherein determining said disease risk yielded by the difference between the measured value and the normal of said LDL concentration parameter the nine

Reply to Office action of July 31, 2007

the measured values and the normal values of the nine atherosclerotic parameters, said method comprising the steps of:

- a measured value,  $c_m$  in mg/dL, of the individual's LDL concentration in human serum is determined using a medical technique for measuring the concentration of blood constituents or said  $c_m$  is determined by the physician,
- a normal value,  $c_n$  in mg/dL, of said LDL concentration is determined by the physician or said  $c_n = 100$  mg/dL for adult,
- substituting said  $c_m$  and said  $c_n$  into the following expression where  $c_m \ge c_n$ :

$$R_1 = \left(\frac{c_m}{c_n}\right)^{\frac{11}{9}} - 1 \tag{1}$$

and

calculating (1) yields—said the disease risk R<sub>1</sub> caused by said the LDL concentration parameter related to the atherosclerotic risk factors being an elevated LDL concentration in human serum, high-fat diet, hypercholesterolemia or

Reply to Office action of July 31, 2007

other risk factors that increase said LDL concentration;

- a measured value, c<sub>m</sub> in mg/L, of the individual's

  CRP concentration in human blood plasma is

  determined using a medical technique for

  measuring the concentration of blood

  constituents or said c<sub>m</sub> is determined by the

  physician,
- a normal value,  $c_n$  in mg/L, of said CRP concentration and an equivalent factor, F, are determined by the physician wherein  $F = \left(\frac{D_c}{D_L}\right)^{\frac{16}{27}}$ ,  $D_C$  = the CRP diffusion coefficient and  $D_L$  = the LDL diffusion coefficient or said  $c_n$  = 1.0 mg/L for adult and said F = 0.66,
- substituting said  $c_m$ , said  $c_n$  and said F into the following expression where  $c_m \ge c_n$ :

$$R_2 = F\left(\left(\frac{c_m}{c_n}\right)^{\frac{11}{9}} - 1\right)$$
 and

calculating (2) yields the disease risk  $R_2$  caused by the CRP concentration parameter

Reply to Office action of July 31, 2007

related to the atherosclerotic risk factors
being an elevated CRP level in human blood
plasma, systemic inflammation, infectious
agents or other risk factors that increase said
CRP level;

- a measured value,  $p_m$  in mmHg, of the individual's blood systolic pressure is determined using a medical technique for measuring the human blood pressure or said  $p_m$  is determined by the physician,
- a normal value,  $p_n$  in mmHg, of said systolic pressure is determined by the physician or said  $p_n = 120$  mmHg for adult,
- substituting said  $p_m$  and said  $p_n$  into the following expression where  $p_m \ge p_n$ :

$$R_3 = \left(\frac{P_m}{P_n}\right)^{\frac{1}{3}} - 1$$
 (3)

and

calculating (3) yields the disease risk R<sub>3</sub>

caused by the systolic pressure parameter

related to the atherosclerotic risk factors

being an elevated level of blood systolic

pressure, family history of hypertension or

Reply to Office action of July 31, 2007

other risk factors that increase said systolic pressure;

- a measured value,  $p_m$  in mmHg, of the individual's blood diastolic pressure is determined using a medical technique for measuring the human blood pressure or said  $p_m$  is determined by the physician,
- a normal value,  $p_n$  in mmHg, of said blood diastolic pressure is determined by the physician or said  $p_n = 70$  mmHg for adult,
- substituting said  $p_m$  and said  $p_n$  into the following expression where  $p_m \ge p_n$ :

$$R_4 = \left(\frac{P_m}{P_n}\right)^{\frac{1}{3}} - 1 \tag{4}$$

and

calculating (4) yields the disease risk R<sub>4</sub>

caused by the diastolic pressure parameter
related to the atherosclerotic risk factors
being an elevate level of blood diastolic
pressure, family history of hypertension or
other risk factors that increase said diastolic
pressure;

Reply to Office action of July 31, 2007

- a measured value,  $f_m$  in  $s^{-1}$ , of the individual's heart rate is determined using a medical technique for measuring the human heart rate or said  $f_m$  is determined by the physician,
- a normal value,  $f_n$  in  $s^{-1}$ , of said heart rate is determined by the physician or said  $f_n = 72$  per minute for adult,
- substituting said  $f_m$  and said  $f_n$  into the following expression where  $f_m > f_n$ :

$$R_s = \left(\frac{f_m}{f_n}\right)^{\frac{2}{9}} - 1$$
and

- by the heart rate parameter related to the atherosclerotic risk factors being an elevated level of heart rate, smoking cigarette, depression or other risk factors that increase said heart rate;
- a measured radius value, a<sub>m</sub> in cm, of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering is determined using a medical

Reply to Office action of July 31, 2007

technique for measuring the sizes of arterial vessels or said am is determined by the physician,

- a normal value,  $a_n$  in cm, of said arterial radius is determined by the physician or said  $a_n = a$  value between 0.2 cm and 2.2 cm for adult,
- substituting said  $a_m$  and said  $a_n$  into the following expression where  $a_m \ge a_n$ :

$$R_6 = \left(\frac{a_m}{a_n}\right)^{\frac{2}{3}} - 1 \tag{6}$$

and

- by the arterial radius parameter related to the atherosclerotic risk factors being an increased size of arterial radius at said lesion-prone sites or other risk factors that increase the size of said arterial radius;
- a measured temperature value, T<sub>m</sub> in °C, of the individual's plasma fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the temperature of human blood plasma or said T<sub>m</sub> is determined by the physician,

Reply to Office action of July 31, 2007

- a normal value,  $T_n$  in °C, of said plasma temperature is determined by the physician or said  $T_n = 37$ °C,
- substituting said  $T_m$  and said  $T_n$  into the following expression where  $T_m \ge T_n$ :

$$R_{7} = \left(\frac{T_{m}}{T_{n}}\right)^{\frac{16}{27}} - 1$$
 (7)

and

- by the plasma temperature parameter related to the atherosclerotic risk factors being an elevated temperature of said human blood plasma at said lesion-prone sites, elevated body temperature-related diseases or other risk factors that increase said plasma temperature;
- a measured value,  $\alpha_m$  in degree, of the angle between gravity and the average velocity of the blood fluid in the region at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $\alpha_m$  is determined by the physician,
- a normal value,  $\alpha_n$  in degree, of said angle is

Reply to Office action of July 31, 2007

determined by the physician or said  $\alpha_n = a$  value between the 10° and 60° for adult,

substituting said  $\alpha_m$  and said  $\alpha_n$  into the following expression where  $\alpha_n \geq \alpha_m$ :

$$R_8 = \left(\frac{\cos \alpha_m}{\cos \alpha_n}\right)^{\frac{2}{9}} - 1 \tag{8}$$

and

- by the angle parameter related to the atherosclerotic risk factors being a reduced size of said angle or other risk factors that reduce said angle size; and
- a measured value,  $z_m$  in cm, of the individual's axial length of diffusion flux along the inner arterial wall at said lesion-prone sites is determined using a medical technique for measuring the human arterial geometries or said  $z_m$  is determined by the physician,
- a normal value,  $z_n$  in cm, of said axial length is determined by the physician or said  $z_n = a$  value between 0.10 cm and 1.00 cm,

substituting said  $z_m$  and said  $z_n$  into the

Page 13 of 25

Reply to Office action of July 31, 2007

following expression where  $z_m \leq z_n$ :

$$R_9 = \left(\frac{z_n}{z_m}\right)^{\frac{2}{9}} - 1 \tag{9}$$

and

calculating (9) yields the disease risk R<sub>9</sub>

caused by the diffusion length parameter

related to the atherosclerotic risk factors

being a decrease in said axial length of the

diffusion flux or other risk factors that

decrease said diffusion length.

Claim 3-10 (canceled)

Claim 11 (currently amended): A method as in slaim 1 having said nine atheroselerotic parameters—caused the nine disease risks and The method of claim 2, further comprising: adding said all nine disease risks  $R_1$  to  $R_9$  together so as to yield a total risk of said disease consisting;

- a current total risk of said disease related to the currently measured values of said atherosclerotic parameters; and
- a previous total risk of said disease related to the previously measured values of said

Reply to Office action of July 31, 2007

atherosclerotic parameters.

Claim 12 (currently amended): A method as in claim 1 having said total risk of said disease and The method of claim 11, further comprising: determining a disease risk level containing said total risk of said disease, said method comprising the steps of:

dividing the disease risk level into the
 following seven risk sublevels: 0.84 ≥ first
 disease risk level ≥ 0.00, 1.75 ≥ second
 disease risk level > 0.84, 2.70 ≥ third disease
 risk level > 1.75, 3.70 ≥ fourth disease risk
 level > 2.70, 4.70 ≥ fifth disease risk level >
 3.70, 5.80 ≥ sixth disease risk level > 4.70
 and seventh disease risk level >5.80; and

selecting a disease risk level containing said total risk of said disease from among seven of said disease risk sublevels.

Claim 13 (currently amended): A method as in claim 1 having said total risk of said disease and The method of claim 11, further comprising: selecting an atherosclerotic risk factor related to

Reply to Office action of July 31, 2007

the atherosclerotic parameter having the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease.

Claim 14 (currently amended): A method as in claim 1 having said LDL concentration parameter—caused the disease risk R<sub>1</sub> and said CRP concentration parameter—caused the disease risk R<sub>2</sub> and The method of claim 2, further comprising: selecting said a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease , said method comprising the steps of:

selecting the LDL mass transfer flux as a primary cause in said disease when said  $R_1 \ge \text{said } R_2$ ; or

selecting the monocyte mass transfer flux as a primary cause in said disease when said  $R_1 < \text{said } R_2$ .

Claim 15 (currently amended): A method as in claim 1 having said LDL concentration parameter—caused the disease risk R<sub>1</sub> and said CRP concentration parameter—caused the disease risk R<sub>2</sub> and The method

Reply to Office action of July 31, 2007

of claim 2, further comprising: selecting said a greater concentration level between the LDL level in the human serum and the CRP level in the human blood plasma so as to result in said greater level as a secondary therapy target, said method comprising the steps of:

- selecting the LDL level in the serum as a secondary therapy target of said disease when said  $R_1 \ge \text{said } R_2$ ; or
- selecting the CRP level in the plasma as a secondary therapy target of said disease when said  $R_1$  < said  $R_2$ .

Claim 16 (currently amended): A method as in elaim 1 having said current total risk of said disease and said previous total risk of said disease and determining said. The method of claim 11, further comprising: determining a relative ratio between said current total risk of said disease and said previous total risk of said disease so as to yield said relative ratio as a therapeutic efficacy of said disease.

Claim 17 (canceled)

Reply to Office action of July 31, 2007

Claim 18 (currently amended): A method as in claim 1, wherein all the methods in said all processes in claim 1 said method has the steps of:

the step 1 of determining the disease risk  $R_1$  yielded by the difference between the measured value  $c_m$  and the normal value  $c_n$  of the LDL concentration parameter wherein  $c_m \geq c_n$  and  $R_1 = \left(\frac{c_m}{c_n}\right)^{\frac{11}{9}} - 1, \text{ determining the disease risk } R_2$ 

yielded by the difference between the measured value  $c_m$  and the normal value  $c_n$  of the CRP concentration parameter wherein  $c_m \ge c_n$  and

$$R_2 = F\left(\left(\frac{c_m}{c_n}\right)^{\frac{11}{9}} - 1\right) \text{ where } F = \left(\frac{D_c}{D_L}\right)^{\frac{16}{27}} , D_C = \text{the CRP}$$

diffusion coefficient and  $D_L$  = the LDL diffusion coefficient, determining the disease risk  $R_3$  yielded by the difference between the measured value  $p_m$  and the normal value  $p_n$  of the blood systolic pressure parameter wherein

$$p_m \ge p_n$$
 and  $R_3 = \left(\frac{P_m}{P_n}\right)^{\frac{1}{3}} - 1$ , determining the disease

risk  $R_4$  yielded by the difference between the measured value  $p_m$  and the normal value  $p_n$  of the blood diastolic pressure parameter wherein

Reply to Office action of July 31, 2007

 $p_m \ge p_n$  and  $R_4 = \left(\frac{P_m}{P_n}\right)^{\frac{1}{3}} - 1$ , determining the disease risk R<sub>5</sub> yielded by the difference between the measured value  $f_m$  and the normal value  $f_n$  of the heart rate parameter wherein  $f_m \ge f_n$  and  $R_s = \left(\frac{f_m}{f_n}\right)^{\frac{2}{9}} - 1$ , determining the disease risk  $R_6$ yielded by the difference between the measured value am and the normal value an of the arterial radius parameter wherein  $a_m \ge a_n$  and  $R_6 = \left(\frac{a_m}{a_m}\right)^{\frac{2}{3}} - 1$ , determining the disease risk  $R_7$ yielded by the difference between the measured value  $T_m$  and the normal value  $T_n$  of the plasma temperature parameter wherein  $T_m \ge T_n$  and  $R_{7} = \left(\frac{T_{m}}{T_{n}}\right)^{\frac{16}{27}} - 1$ , determining the disease risk  $R_{8}$ yielded by the difference between the measured value  $\alpha_m$  and the normal value  $\alpha_n$  of the angle parameter wherein  $\alpha_n \ge \alpha_m$  and  $R_s = \left(\frac{\cos \alpha_m}{\cos \alpha}\right)^{\frac{1}{9}} - 1$ , and determining the disease risk R9 yielded by the difference between the measured value zm and the normal value  $z_n$  of the diffusion length parameter wherein  $z_n \ge z_m$  and  $R_9 = \left(\frac{z_n}{z_n}\right)^{\frac{2}{9}} - 1$ ;

Page 19 of 25

Reply to Office action of July 31, 2007

the step 2 of adding all said nine disease risks

R<sub>1</sub> to R<sub>9</sub> in the step 1 together so as to yield a total risk of said disease consisting of a current total risk of said disease related to the currently measured values of the atherosclerotic parameters and a previous total risk of said disease related to the previously measured values of the atherosclerotic parameters;

the step 3 of selecting a disease risk level

containing said total risk of said disease in
the step 2 from following among seven of the
disease risk sublevels: 0.84 ≥ first disease
risk level ≥ 0.00, 1.75 ≥ second disease risk
level > 0.84, 2.70 ≥ third disease risk level >
1.75, 3.70 ≥ fourth disease risk level > 2.70,
4.70 ≥ fifth disease risk level > 3.70, 5.80 ≥
sixth disease risk level > 4.70 and seventh
disease risk level > 5.80;

the step 4 of selecting an atherosclerotic risk
factor related to an atherosclerotic parameter
having the greatest contribution to said total
risk of said disease in the step 2 so as to
result in said risk factor as a primary therapy

Reply to Office action of July 31, 2007

## target of said disease;

- the step 5 of selecting the LDL mass transfer flux as a primary cause in said disease when said  $R_1$  in the step 1  $\geq$  said  $R_2$  in the step 1 or selecting the monocyte mass transfer flux as a primary cause in said disease when said  $R_1 <$  said  $R_2$ ;
- the step 6 of selecting the LDL level in human serum as a secondary therapy target of said disease when said  $R_1$  in the step  $1 \ge$  said  $R_2$  in the step 1 or selecting the CRP level in human blood plasma as a secondary therapy target of said disease when said  $R_1 <$  said  $R_2$ ; and
- the step 7 of determining a relative ratio

  between said current total risk of said disease
  in the step 2 and said previous total risk of
  said disease in the step 2 so as to yield said
  relative ratio as a therapeutic efficacy of
  said disease; and
- wherein said step 1 through said step 7 are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device

Reply to Office action of July 31, 2007

to accomplish said method and to output a result of said method to a display or a memory or another computer on a network, or to a user comprising:

starting the MMA.exe program on said device;

inputting the currently measured values, the previously measured values and the normal values of the individual's atherosclerosis parameters into the input screen of said MMA.exe by using the keyboard of said device;

clicking the "update" button and the "calc. risk" button of said input screen;

clicking the "evaluate" button of the MMA.exe output screen; and

outputting said output screen to a display or a memory or another computer on a network, or to a user by using said computer device so as to produce a result of said methods, called the screening report containing a total risk of said disease, a disease risk level, a primary cause in said disease, a primary therapy target of said disease, a secondary therapy target of

Reply to Office action of July 31, 2007

said disease and a therapeutic efficiency, to an individual who requires the diagnosis, the prevention or the treatment of atherosclerosis-related CHD or stroke or other cardiovascular disease.

Claim 19 (new): The method of claim 18, further comprising: repeating said method accomplished by using said device until the individual's disease risk level is reduced to a normal level for said individual who requires the therapy to prevent or to treat atherosclerosis-related CHD or stroke or other cardiovascular disease.